REMARKS

1. Claim Objections

Applicants have made the appropriate correction and request withdrawal of this objection.

2. Rejections under 35 U.S.C. 102(b)

2.1 Grieshaber et al.

Claims 1, 2, and 3 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Grieshaber et al. Endocrinology, vol. 141, 20002 (hereinafter Grieshaber et al).

To anticipate a claim, the reference must teach every element of the claim, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)."

The Examiner asserts that Grieshaber et al discloses a method of examining undifferentiated granulosa cells exposed to FSH and then concludes that this disclosure anticipates the claimed subject matter.

Applicants respectfully disagree with the Examiner's conclusion.

Grieshaber discloses an experiment in which rat ovarian granulosa cells were incubated in the presence or absence of FSH or activating or inhibitory drugs. The cells were then measured for actin, cAMP, and Ca^{2+} levels. The results indicated that FSH induced changes in the cell morphology and cell-to-cell interactions, and that the structural changes likely involved the actin cytoskeleton (p3463 col. 1). The authors further concluded that the adenyl cyclase signal, in particular the /cAMP signal is responsible for FSH-dependent granulosa cell differentiation of filopodia and lamellopdia formation.

Grieshaber et al only observes production of cAMP and reorganization of the actin cytoskeleton when cells are exposed to FSH, and does not address the expression of either Class I β-tubulin, tropomyosin-4, or kinesin heavy chain genes. Claims 1-3 of the instant application recite a method of altering the regulation of expression of a gene selected from Class I β-tubulin, tropomyosin-4, and kinesin heavy chain by contacting the gene with an effective amount of FSH. Therefore Grieshaber et al does not explicitly teach a method of altering gene expression of the genes claimed in the instant application.

Furthermore, the Examiner asserts that because Grieshaber et al discloses the important role FSH plays in granluosa cell differentiation and follicular development that this reference anticipates the instant claims. Although the Grieshaber et al discloses that FSH exposure induces changes in cell differentiation, it is not inherent from the disclosure that the expression of Class I β-tubulin, tropomyosin-4, and kinesin heavy chain are regulated by FSH. Grieshaber et al merely discusses the morphological changes of the granulosa cells and production of cAMP when the cells are treated with FSH, but fails to discuss any specific genes that are regulated by FSH.

The instant application discloses methods in which FSH regulated the expression of specific cytoskeleton genes. As claimed Class I β-tubulin, tropomyosin-4, and kinesin heavy chain are among the specific genes of the cytoskeleton regulated by FSH. Furthermore as discussed below, the methods of regulating the genes of the instant application are not inherent from Grieshaber et al as other similar experiments by others yielded dissimilar results.

Grieshaber et al fails to teach all of the elements of the claims either explicitly of inherently. As such, Grieshaber et al does not anticipate the claimed invention. Accordingly the

rejection of claims 1 – 3 under 35 U.S.C. § 102(b) as allegedly being anticipated by Grieshaber et al. has respectfully been traversed.

2.2 Ben-Ze'ev et al

The Examiner rejected claims 1, and 2 under 35 U.S.C. 102(b) as allegedly being anticipated by Ben-Ze'ev et al Journal of Biological Chemistry, vol. 262, 1987 (hereinafter Ben-Ze'ev et al).

This rejection is respectfully traversed as follows.

Claims 1-3 of the instant application recite a method of altering the regulation of expression of Class I β-tubulin, tropomyosin-4, or kinesin heavy chain by contacting the gene with an effective amount of FSH. The instant specification shows β-tubulin levels dramatically affected by FSH treatment (see Fig. 4).

The Examiner asserts that Ben-Ze'ev teaches a method of treating β-tubulin containing granulosa cells with FSH.

Applicants respectfully disagree with the Examiner's assertion that Ben-Ze'ev anticipates the instant claims.

Ben-Ze'ev et al discloses methods of treating cells with FSH and observing expression of cytoskeletal proteins. Ben-Ze'ev et al does not show an alteration of expression of any of the claimed proteins. Ben-Ze'ev et al teaches no alteration of β-tubulin synthesis in cells exposed to FSH. In contrast to the instant claims, Ben-Ze'ev concludes, "By analyzing the labeling of ά- and β-tubulin in the Triton x-100 and high salt-soluble fraction, which contained all of the tubulins and no vimentin, we found the same levels of ά- and β-tubulin synthesis in control and in FSH-treated cells." (page 5370 last paragraph).

Therefore, the methods disclosed by Ben-Ze'ev clearly show no alteration in β-tubulin levels, nor do they teach any alteration of expression in the tropomyosin-4 or kinesin heavy chain proteins as recited in the claims.

Accordingly, the rejection of claims 1 and 2 under 35 U.S.C. § 102(b) over Ben-Ze'ev et al. is respectfully traversed.

2.3 Closucard-Martinato et al

The examiner rejected claims 1 and 2 under U.S.C. 102 (b) as allegedly being anticipated by Clouscard-Martinato et al Animal Genetic, vol. 29, 1998 (hereinafter Clouscard-Martinato et al).

Applicants respectfully traverse this rejection as follows.

As an initial matter, the Examiner concedes that the reference fails to disclose the genes as claimed in the application. The Examiner asserts that the presence of the genes recited in the claims must be inherent. Applicants respectfully disagree with this conclusion.

Clouscard-Martinato et al discloses isolation of FSH-regulated genes from Pig granulosa cells using mRNA differential display. The reference teaches that most of the genes tested were unaffected by FSH treatment, "Therefore, this low percentage can be explained by a low frequency of genes responding to FSH-treatment in the present authors' cell culture model" (p.103 col. 2 and p.104 col. 1). Thus, Clouscard-Martinato teaches that FSH exposure does not regulate expression in all granulosa genes but only a small percentage of specific genes. Moreover, Clouscard-Martinato does not disclose the specific genes of the instant application.

The subject matter of the instant application is a method of altering the regulation of expression of a specific gene or genes by contacting the gene with an effective amount of FSH, alleging the mere existence of a particular gene does not disclose altering its gene expression.

Clouscard-Martinato et al does not explicitly or inherently teach altering the expression of the genes as claimed.

As such, Clouscard-Martinato et al fails to anticipate the claims. Accordingly the rejection of claims 1 and 2 under 35 U.S.C. § 102(b) over Clouscard-Martinato et al. has respectfully been traversed.

3. Rejections under 35 U.S.C. 103(a)

3.1 Ben-Ze'ev et al or Clouscard-Martinato or Grieshaber et al in view of Kimble et al, Sbdonline and pbil.

Claims 1-3 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentably obvious over Ben-Ze'ev et al or Clouscard-Martinato or Grieshaber as supportable by Kimble et al Genetic, vol. 126, 1990 (hereinafter Kimble et al), along with http://www.sdbonline.org/fly/cytoskel/tubet1-1.htm (hereinafter sdbonline) and http://pbil.univ-lyon1.fr/cgi-bin/acnuc-search-id?query=TPM4_RAT&db=Hoverprot&ide...(hereinafter pbil).

Applicants respectfully traverse this rejection for the reasons stated above and in addition for the reasons stated as follows.

The Examiner concedes that neither of the primary or secondary references teaches altering the regulation of gene expression of the claimed genes, β-tubulin, tropomyosin-4 or kinesin heavy chain.

Kimble and the sbdonline web page are cited by the Examiner as allegedly teaching the importance of the β-tubulin gene in cytoskeletal reorganization. The Examiner asserts that the pbil web site is cited to teach that the tropomyosin-4 gene is a well-known cytoskeletal gene.

None of the aforementioned references discusses the kinesin heavy chain gene or a method of altering expression of the claimed genes. As such neither Kimble, sbdonline nor the University of Lyon website cure the deficiencies of the other prior art references.

The Examiner argues that it would allegedly have been obvious to one having ordinary skill in the art to contact granulosa cells with FSH and expect to see alteration of genes associated with the cytoskeleton. Applicants respectfully submit that this argument is flawed as it fails to appreciate the subject matter of the instant application.

The subject matter of the instant application is a method of altering the regulation of expression of a specific gene or genes by contacting the gene with an effective amount of FSH. None of the cited references teaches altering the expression of the genes as claimed.

Moreover, as discussed above, the studies performed in Ben-Ze'ev et al resulted in no alteration of β-tubulin when granulosa cells where exposed to FSH, therefore Ben Ze'ev et al actually teaches away from inherently altering β-tubulin when a granulosa cell is exposed to FSH. Therefore, Ben-Ze'ev et al teaches that it would not have been obvious to see alterations in all cytoskeletal genes when exposed to FSH.

Accordingly the rejection under 35 U.S.C §103(a) as allegedly being unpatentable over Ben-Ze'ev et al or Clouscard-Martinato et al or Grieshaber et al as supported by Kimble et al along with the sdbonline article and the pbil citation is respectfully traversed.

It is respectfully submitted that the amendments above place the application in condition for allowance, an early notification thereof being earnestly solicited. However, if any issues remain outstanding, the Examiner is respectfully requested to contact the undersigned so the prosecution may be expedited. To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the

filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

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